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BioPharma Services
News

BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

Making liquid biopsy a reality for patients

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Patients with advanced cancer can have in general a poor prognosis, however, for many patients whose tumours harbour certain specific molecular alterations, targeted therapy and/or immunotherapy provide significant improvement in survival and quality of life. Accordingly, patients with advanced cancer in which these targetable molecular alterations typically occur, should receive the molecular testing required to identify them, and based on the outcome, should receive appropriate personalised treatments.

In 2019, Eurofins Genoma together with one of their pharma customers recruited specialists in the fields of oncology, diagnosis, and treatment of breast cancer, to start a joint working group to systematically assess the evidence supporting the clinical utility of molecular analysis on breast cancer patients. The NGBreast project recruited 80 specialists from every Italian region to learn the best clinical practice in terms of which breast cancer patients and samples should be tested, which genes should be analysed, and how these tests should be designed, validated, and performed.

The recruited specialists were trained in small classes. The whole project included four educational meetings with the final aim of learning how to best manage liquid biopsy in profiling breast cancer patients. After the training sessions, 1,500 liquid biopsies and 500 tissue profiling tests were made available to the specialists who attended the training. Both tests were performed using NGS and are part of the Onconext™ product range already commercialised by Eurofins Genoma. A tailor-made online portal was developed to support the specialists participating in the NGBreast project, providing access to information and training material, as well as facilitating easy ordering of the different tests.

This kind of approach is the first of its kind in trying to make liquid biopsy a reality in daily clinical practice. Due to the success of the 2019 edition, the NGBreast project will continue in 2020 with new class trainings, educational meetings, and on-the-job workshops. For more information, visit: *www.onconext.it/en/onconext-liquid/; www.ngbreast.it/*

Nitrosamine Impurities in pharmaceutical products – a "burning" topic for the industry

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N-nitrosamines are a family of well-known impurities and are included in the "cohort of concerns" list in the ICH-M7 guideline, as their intake can be associated with significant carcinogenic risk.

In 2018, traces of N-nitrosodimethylamine (NDMA) and N-Nitrosodiethylamine (NDEA) found in some sartans active pharmaceutical ingredients (APIs) caused several market recalls. In a later phase, detection of these impurities in other classes of medicine, such as ranitidine and metformin, raised additional concerns about patient safety.

The FDA and the EMA are driving the regulatory review and defining new requirements: temporary limits for most common nitrosamines are currently being set based upon the Maximum Daily Intake; European Pharmacopoeia monographs are also being updated to include new mandatory tests for five sartans. The general expectation is that limits will be further lowered in the future in a move towards an ideal absence of these compounds.

Investigations reveal that, in addition to the use of nitrosating agents, secondary amines and contaminated materials, impurities could also be associated with the use of recovered solvents and cross-contamination when different processes run on the same line. The EMA committee does not exclude that additional sources could be identified in the future.

In this context, the EMA and other regulatory authorities asked all Marketing Authorisation Holders to review all products containing chemical-synthetised APIs: in case the initial risk-assessment of the manufacturing processes cannot exclude potential contamination, this has to be followed by confirmatory analysis of the product. Testing can be challenging due to low limits and complex matrices. Positive results must be immediately communicated to competent authorities in order to agree on contamination control strategies.

Manufacturing Authorisation Holders (MAHs) can also benefit from a transition period of up to two years to apply for variations in processes, specifications, and finally ensure complete risk mitigation.

Eurofins BioPharma Product Testing network of GMP labs has the capability and capacity to assist clients through all the steps of the investigation process–from initial risk assessment to analytical methods validation and from screening and confirmatory testing to routine quality control in order to confirm nitrosamine levels in drug substances and drug products. For more information, visit: *www.eurofinsus.com/bpt*

Quality by Design – A systemic approach to process development

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Quality by Design (QbD) is an essential concept that one should apply during the development of drug substances that are in late-stage clinical trials. By deploying a QbD approach, Eurofins CDMO enables clients to build the required quality into the product during the design and development phase by understanding the effects of material attributes and process parameters on Critical Quality Attributes (CQAs).

Eurofins CDMO's approach typically includes: setting quality objectives (QTPPs); identifying CQAs; prioritising process parameters and material attributes using Failure Modes and Effects Analysis (FMEA); screening Design of Experiment (DOE) to derive Critical Process Parameters (CPPs) and Critical Material Attributes (CMAs); optimising Response Surface Methodologies (RSM); arriving at design space; and lastly, utilising control strategies to regulate CPPs in order to achieve high process capability.

Eurofins CDMO strongly believes in the importance of effective QbD during the process development and involves a cross-functional team of analysts, process engineers, quality assurance, sourcing and manufacturing experts that help to consider right input variables during designing and developing the process. Cumulative wisdom of the brainstorming team during FMEA ensures more robust processes and methods, resulting in improved efficiency, reduced risk, and fewer failures. This also enables the team to achieve one of the elements of the ICH Q10 Pharmaceutical Quality System: continual improvement within the boundaries of design space with minimum regulatory consent to the customer.

For more information: *www.eurofins.com/biopharma-services/cdmo/*

Eliminating donor variability in ADCC Assays – implementation in QC Lot Release

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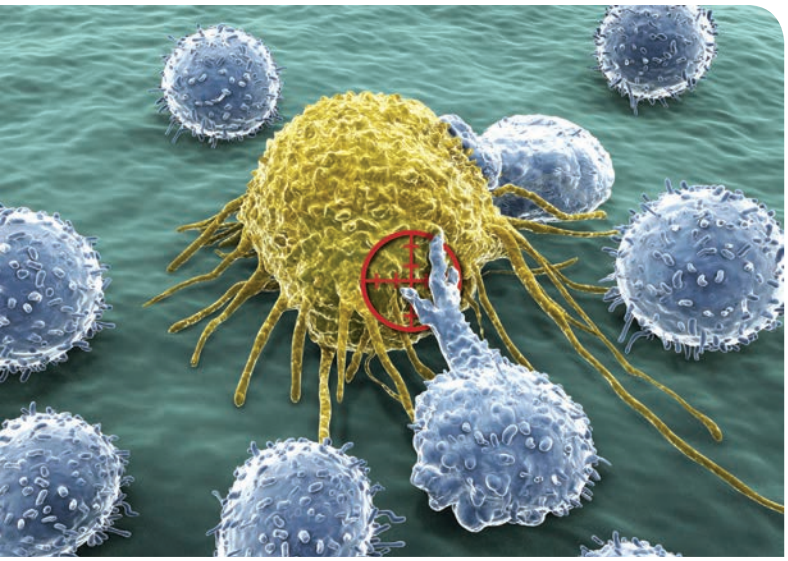
Class I therapeutic antibodies achieve their clinical efficacy by binding to their target antigen and through Fragment crystallisable region (Fc) domain-mediated recruitment of immune cell effectors to attack and kill the target cell. Therefore, developers of such therapeutic antibodies must assess all possible Fc-mediated mechanisms of action of their molecules, including Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC). The ADCC assays are one of the most challenging assays to implement for lot release testing. The success of these assays is highly dependent on the quality of immune effector cells, e.g. most commonly used primary human cells, such as peripheral blood mononuclear cells (PBMCs) or natural killer (NK) cells, and often suffer from inherent donor variability resulting in high assay failure rates.



Eurofins DiscoverX introduced single donor-derived immune effector cells, the KILR® CD16 Effector Cells, to address these challenges, and these cells can be used in any ADCC assay that directly measures target cell death in a co-culture model. These effector cells are human Cytotoxic T-lymphocytes (CD3+/CD8+) that have been stably transfected with human CD16 receptor (FcγIIIa V158). The cells deliver very low background killing, resulting in robust assay windows with excellent repeatability and precision. The patented manufacturing process ensures consistent assay performance across multiple lots. These cells can be maintained in culture for 14 days with no loss in killing capability, thereby delivering ultimate assay design flexibility. An independent study conducted by a large global CRO using ADCC models for rituximab demonstrated these cells to be a suitable system for QC lot release, and they are now actively recommended to their clients.

Eurofins DiscoverX delivers enabling technologies and the most comprehensive portfolio of established biochemical and cell-based assays, cell lines, reagents, and custom assay development services that accelerate multi-modality drug development programmes from discovery to QC lot release. For more information visit: *www.discoverx.com/products-applications/kilr-cytotoxicity-assays*

Eurofins Viracor creates separate BioPharma Services Business

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Eurofins Viracor is excited to announce that as a result of the continued growth of both its Clinical Diagnostics and BioPharma Services businesses, Eurofins Viracor BioPharma Services has become a new legal entity, under Eurofins Scientific, as of 1 January, 2020.

With the impetus to operate both businesses at the highest level of customer service, this formal separation within the organisation enables the new entity to more fully focus, as a standalone business, on supporting its growing strategic BioPharma client partnerships – helping advance new therapies to market by expanding and enhancing timely, high-quality and accurate testing services across multiple phases of drug development.

Scott Mattivi, General Manager, will continue to lead Eurofins Viracor BioPharma Services to safeguard the rigorous scientific and quality standards that drug development companies have come to rely on for their clinical study needs.

“Our teams partner collaboratively with our sponsors to solve some of the toughest bioassay challenges, using our unique combination of state-of-the-art technology and extensive specialised expertise,” says Scott. “We are inspired every day to perform better, knowing patients are waiting for our timely, accurate, and sometimes life-saving test results.”

With location and contact information remaining the same, the only changes clients may notice will be a change to the logo on various communications. And visitors to the viracor-eurofins.com website will see incremental changes, as the companies move toward separate but linked sites for the Clinical Diagnostic and BioPharma businesses.

Eurofins Viracor BioPharma Services and Eurofins Viracor look forward to continued successful partnerships with its valued clients.

For more information, visit: *www.viracor-eurofins.com/*

Considerations for selecting your partner for Biologics Characterisation

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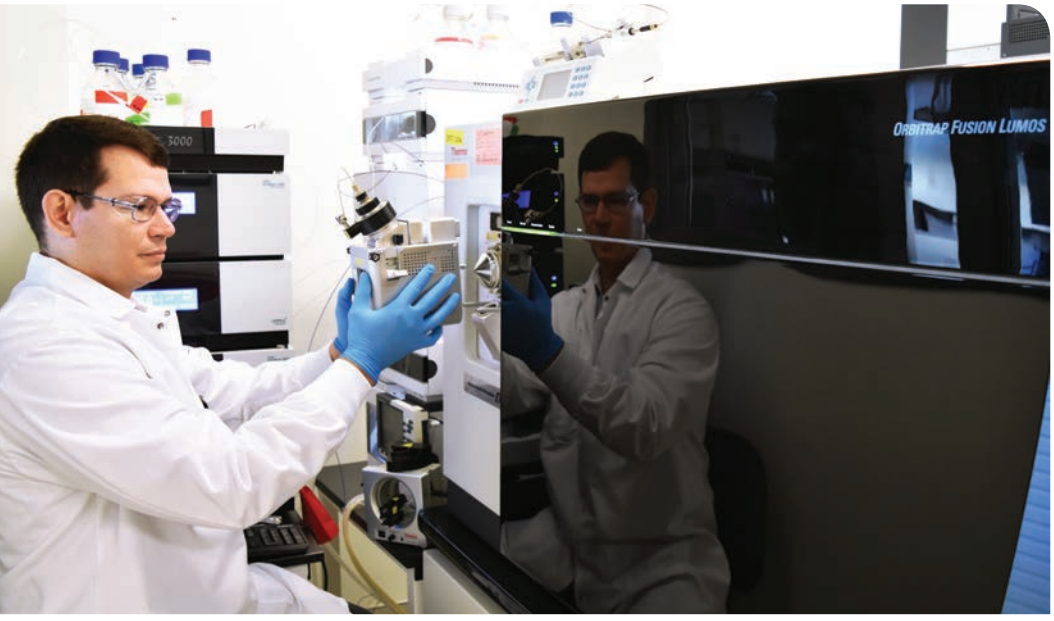
Throughout the course of product development, Biopharma companies need to consider multiple outsourcing plans, ranging from very early discovery support to late phase stability and release programmes. When selecting a provider for their Biologics characterisation needs, companies often consider reputation, expertise, and state-of-the-art instrumentation. At this stage of the product development, compliance generally ranks low on the priority list; however, this criterion should be carefully reconsidered.



Even if companies first encounter the need for characterisation at an early stage of their product development, in the pre-Investigational New Drug space, the application of these complex techniques is certainly not limited to pre-clinical/R&D phases.

Characterisation methods are an integral part of the qualification or re-qualification of Reference Standards (RS) throughout the entire development cycle. These methods are included in RS management programmes, including post-approval ones. Since they are part of the application, data integrity requirements apply to any of the information provided to the agency for review and sustaining the use of a new RS lot.

Characterisation methods will also be required for any comparability study at each of the phases where critical changes are made. For example, if the major changes happen to be made after pivotal clinical trials or after commercial approval, the characterisation methods will be part of a critical data set. At this stage, the regulatory bodies are all in agreement: characterisation assays need to be demonstrated fit-for-purpose at a level equivalent to what is in essence an R&D validation. The concepts applied to this demonstration of fitness are equivalent to the elements of a validation, including specificity, sensitivity and repeatability.

Even though the regulatory agencies are not going to expect full cGMP compliance for these complex methods, it is also clear that these R&D assays cannot be performed by documenting them on the back of a napkin either – far from it.

Biopharma organisations might therefore be prudent to consider items such as data integrity, documentation management, and instrument performance management when choosing an outsourcing partner, which will guarantee that the investment they make in the very early stages of their product's development is a robust and fruitful one. Thanks to its long history of providing a high level of regulatory compliance, including for complex assays, Eurofins Biopharma Product Testing is a trusted partner in biologics characterisation outsourcing. For more information, visit: *www.eurofins.com/biopharma-services/product-testing/*

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